ORIGINAL RESEARCH PAPER

Orthopaedics

RHEUMATOID ARTHRITIS

KEY WORDS:

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ABSTRACT

Rheumatoid arthritis is characterized by a persistent joint inflammation along with cartilage and bone damage with significant limitation of activity, reduction in the quality of life and often systemic complications. As the treatment of RA is of long duration and often leads to new complications, the treatment should be to halt these complications and to improve quality of life of patient, so, this study is to highlighten the newer recommendations for treating patients with RA as per lastest recommendations from American college of Rheumatology.

INTRODUCTION

RA is a multisystemic, chronic, autoimmune disorder of unknown cause. Although there are a variety of systemic manifestations, the major characteristic feature is chronic, symmetrical and erosive synovitis, involving peripheral joints, usually. Most of the patients have elevated titres of serum rheumatoid factors. Despite destructive potential, the course of RA can be quite variable. Some patients may experience only a mild oligoarticular illness of brief duration with minimal joint damage, whereas others can have a progressive polyarthritis with marked functional impairment and disability. Associated non-articular manifestations may include subcutaneous nodules, vasculitis, pericarditis, pulmonary nodules or intestinal fibrosis, mononeuritis multiplex, episcleritis or scleritis[1].

Definition

Epidemiological studies of RA are dependent on the criteria used to define the disease. This is challenging, because no aetiological agent has been identified and there are no unique clinical or laboratory features that can be used to define the disease clearly. Therefore, diagnosis is based on the presence or absence of combinations of clinical, laboratory and radiological abnormalities. Unfortunately, these assessments are prone to measurement error[1].

Epidemiology

In the GBD 2017 data, the age-standardized prevalence of RA was higher in North America (0.38%; 95% CI 0.36–0.40%), western Europe (0.35%; 95% CI 0.31–0.38%) and the Caribbean (0.34%; 95% CI 0.30–0.37%) than in Oceania (0.14%; 95% CI 0.12–0.15%), western sub-Saharan Africa (0.13%; 95% 0.11–0.15%) or southeast Asia (0.10%; 95% CI 0.089–0.11%)[2].

A 2021 meta-analysis of 67 RA-cohort incidence and prevalence studies from 41 countries found a pooled prevalence of 0.46% (95% CI 0.37–0.57%) for the period 1986–2014[3]. Although this estimate is almost twice the 2017 global prevalence of 0.27% (95% CI 0.24–0.3%) found in the GBD study[2,4].

In India, Rheumatoid arthritis (RA) affects about 0.92% of the adult population[5]. Studies in India reported a prevalence range from 0.28% to 0.7%. In a study conducted in the year 1996 in the Bhigwan village of Pune district using surveys developed by WHO and International League of associations for Rheumatology (WHO-ILAR) Community Oriented Program for Control of Rheumatic Diseases (COPCORD) reported a prevalence of 0.51% for RA diagnosed with ACR criteria and 0.6% for RA diagnosed clinically[6]. In Jammu, a prevalence of 0.7% was reported by Mahajan et al[7]. In Ballabhgarh (Haryana) prevalence reported was 0.7%[8].

Risk factors

Sex hormones, menstrual and reproductive factors:

Despite the inability to provide country-specific incidence data, the above-mentioned studies have generated some provocative observations regarding sex hormones as predisposing factors.

The obvious predominance of RA in the female gender has initiated an interest in examining the association of menstrual, hormonal and reproductive factors with the development of RA. For example, several studies have indicated that nulliparity is a risk factor for RA [9]. It is also well established that pregnancy is associated with remission of RA, and exacerbations are common during the postpartum period [10, 11]. Following the first reports by Wingrave and Kay in 1978 [12], there have been multiple studies examining the possible protective effect of oral contraceptives against the development of RA. These studies represent the entire repertoire of investigational methods in epidemiology, and though none of these studies is conclusive, there seems to be a consensus that oral contraceptives protect or postpone the development of severe RA [13].

Genetic Factors

Several lines of evidence suggest that genetic factors other than gender play a role in development of RA.

Family studies indicate a genetic predisposition for RA. Severe RA is found at approximately four times the expected rate in first-degree relatives of individuals with disease associated with the presence of rheumatoid factor, and ~10% of patients with RA have an affected first-degree relative [14]. Furthermore, monozygotic twins are at least four times more likely to be concordant for RA than dizygotic twins, who have a similar risk of developing RA as non-twin siblings, while only 15–20% of monozygotic twins are concordant for RA [15]. However, this also implies that factors other than genetics play an important aetiopathogenic role.

One of the major genetic factors in the aetiology of RA is the class II major histocompatibility complex (MHC) gene product HLA-DR4 [16]. As many as 70% of patients with classic or definite RA express HLA-DR4, compared with 28% of control individuals. An association with HLA-DR4 has been noted in many populations, including North American and European whites, Chippewa Indians, Japanese and native populations in India, Mexico, South America and southern China. However, in a number of groups, including Israeli Jews, Asian Indians and Yakima Indians of North America, there is no association between the development of RA and HLA-DR4. In the former two groups, there is an association between RA and HLA-DR1; and in the latter two groups, there is an association with HLA-Dw16. These observations form the basis for the suggestion that shared epitopes determine susceptibility to RA [17].

Other Factors

In addition to age- and sex-related predisposing factors, a

number of other factors, including socio-economic status [17], education [19] and stress [20], have been suggested to play predisposing roles.

Clinical presentation[22]:

Once the disease process of RA is established, the wrists, metacarpophalangeal (MCP), and proximal interphalangeal (PIP) joints stand out as the most frequently involved joints. Distal interphalangeal (DIP) joint involvement may occur in RA, but it usually is a manifestation of coexistent osteoarthritis. Flexor tendon tenosynovitis is a frequent hallmark of RA and leads to decreased range of motion, reduced grip strength, and "trigger" fingers. Progressive destruction of the joints and soft tissues may lead to chronic, irreversible deformities. Ulnar deviation results from subluxation of the MCP joints, with subluxation of the proximal phalanx to the volar side of the hand. Hyperextension of the PIP joint with flexion of the DIP joint ("swan-neck deformity"), flexion of the PIP joint with hyperextension of the DIP joint ("boutonnière deformity"), and subluxation of the first MCP joint with hyperextension of the first interphalangeal (IP) joint ("Z-line deformity") also may result from damage to the tendons, joint capsule, and other soft tissues in these small joints. Inflammation about the ulnar styloid and tenosynovitis of the extensor carpi ulnaris may cause subluxation of the distal ulna, resulting in a "piano-key movement" of the ulnar styloid. While metatarsophalangeal joint (MTP) involvement is a feature of early disease in the feet, the ankle and midtarsal regions are usually affected later in the course of disease and often predispose to pes planovalgus ("flat feet"). Large joints, including the knees and shoulders, are often affected in established disease, although these joints may remain asymptomatic for many years after onset. Atlantoaxial involvement of the cervical spine is clinically noteworthy because of its potential to cause compressive myelopathy and neurologic dysfunction. Neurologic manifestations are rarely a presenting sign or symptom of atlantoaxial disease, but they may evolve over time with progressive instability of C1 on C2. The prevalence of atlantoaxial subluxation has been declining in recent years, and occurs now in less than 10% of patients. Unlike the spondyloarthritides, RA does not affect the thoracic and lumbar spine except in very unusual circumstances. Radiographic abnormalities of the temporomandibular joint occur commonly in patients with RA, but they are rarely associated with significant symptoms or functional impairment.

Extraarticular manifestations may develop during the clinical course of RA, even prior to the onset of arthritis. Patients most likely to develop extraarticular disease have a history of smoking, early onset of significant physical disability, and test positive for serum RF. Subcutaneous nodules, secondary Sjögren's syndrome, pulmonary nodules, and anemia are among the most frequently observed extraarticular manifestations. Recent studies have shown a decrease in the incidence and severity of at least some extraarticular manifestations, particularly Felty's syndrome and vasculitis.

Management

Early diagnosis and treatment in RA is associated with improved outcomes and is thus an important overarching principle in its management[22].

The first line of drug for rheumatoid arthritis remains DAMARDs and hence the treatment is based upon the response to DMARDs. The recommendations are based upon guidelines by American college of rheumatology[23] and are as follows:

Recommendations for DMARD-naive patients with moderate-to-high disease activity

a. DMARD monotherapy

- Methotrexate is strongly recommended over hydroxychloroquine or sulfasalazine for DMARD naive patients with moderate-to-high disease activity
- Methotrexate is conditionally recommended over leflunomide for DMARD-naive patients with moderate-to-high disease activity
- Methotrexate monotherapy is strongly recommended over bDMARD or tsDMARD monotherapy for DMARD-naive patients with moderate-to-high disease activity
- Methotrexate monotherapy is conditionally recommended over dual or triple csDMARD therapy for DMARD-naive patients with moderate-to-high disease activity
- Methotrexate monotherapy is conditionally recommended over methotrexate plus a tumor necrosis factor (TNF) inhibitor for DMARD-naive patients with moderate-to-high disease activity
- Methotrexate monotherapy is strongly recommended over methotrexate plus a non–TNF inhibitor bDMARD or tsDMARD for DMARD-naive patients with moderate-to-high disease activity

b. Glucocorticoids

- Initiation of a csDMARD without short-term (<3 months) glucocorticoids is conditionally recommended over initiation of a csDMARD with short-term glucocorticoids for DMARD-naive patients with moderate-to-high disease activity
- Initiation of a csDMARD without longerterm (≥3 months) glucocorticoids is strongly recommended over initiation of a csDMARD with longer-term glucocorticoids for DMARD-naive patients with moderate-to-high disease activity

Recommendations For Dmard-naive Patients With Low Disease Activity

- Hydroxychloroquine is conditionally recommended over other csDMARDs, sulfasalazine is conditionally recommended over methotrexate, and methotrexate is conditionally recommended over leflunomide for DMARDnaive patients with low disease activity

Recommendation for patients who have been treated with csDMARDs, excluding methotrexate, and who have moderate-to-high disease activity

- Methotrexate monotherapy is conditionally recommended over the combination of methotrexate plus a bDMARD or tsDMARD

Recommendations For Administration Of Methotrexate

- Oral methotrexate is conditionally recommended over subcutaneous methotrexate for patients initiating methotrexate
- Initiation/titration of methotrexate to a weekly dose of at least 15 mg within 4 to 6 weeks is conditionally recommended over initiation/ titration to a weekly dose of
- A split dose of oral methotrexate over 24 hours or weekly subcutaneous injections, and/or an increased dose of folic/folinic acid, is conditionally recommended over switching to alternative DMARD(s) for patients not tolerating oral weekly methotrexate
- Switching to subcutaneous methotrexate is conditionally recommended over the addition of/ switching to alternative DMARD(s) for patients taking oral methotrexate who are not at target

Recommendations For Treatment Modification In Patients Treated With Dmards Who Are Not At Target

- Treat-to-target A treat-to-target approach is strongly recommended over usual care for patients who have not been previously treated with bDMARDs or tsDMARDs
- A treat-to-target approach is conditionally recommended over usual care for patients who have had an inadequate response to bDMARDs or tsDMARDs
- A minimal initial treatment goal of low disease activity is conditionally recommended over a goal of remission

Modification of DMARD(s)

- Addition of a bDMARD or tsDMARD is conditionally recommended over triple therapy (i.e., addition of sulfasalazine and hydroxychloroquine) for patients taking maximally tolerated doses of methotrexate who are not at target
- Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients taking a bDMARD or tsDMARD who are not at target

Use Of Glucocorticoids

- Addition of/switching to DMARDs is conditionally recommended over continuation of glucocorticoids for patients taking glucocorticoids to remain at target
- Addition of/switching to DMARDs (with or without intraarticular [IA] glucocorticoids) is conditionally recommended over the use of IA glucocorticoids alone for patients taking DMARDs who are not at target

Recommendations for tapering/discontinuing DMARDs

- Continuation of all DMARDs at their current dose is conditionally recommended over a dose reduction of a DMARD, dose reduction is conditionally recommended over gradual discontinuation of a DMARD, and gradual discontinuation is conditionally recommended over abrupt discontinuation of a DMARD for patients who are at target for at least 6 months
- Gradual discontinuation of sulfasalazine is conditionally recommended over gradual discontinuation of hydroxychloroquine for patients taking triple therapy who wish to discontinue a DMARD
- Gradual discontinuation of methotrexate is conditionally recommended over gradual discontinuation of the bDMARD or tsDMARD for patients taking methotrexate plus a bDMARD or tsDMARD who wish to discontinue a DMARD

CONCLUSION

In conclusion, the recent onset rheumatoid arthritis is an important issue which can have good prognosis if diagnosed and managed timely. However, the progressive course and subsequent development of RA an joint destruction would be expected to be observed in a substantial proportions of these patients. Identification of associated factors of persistent disease or predictive factors of RA development requires a complete clinical examination and rational use of serological test and hence should be treated accordingly.

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